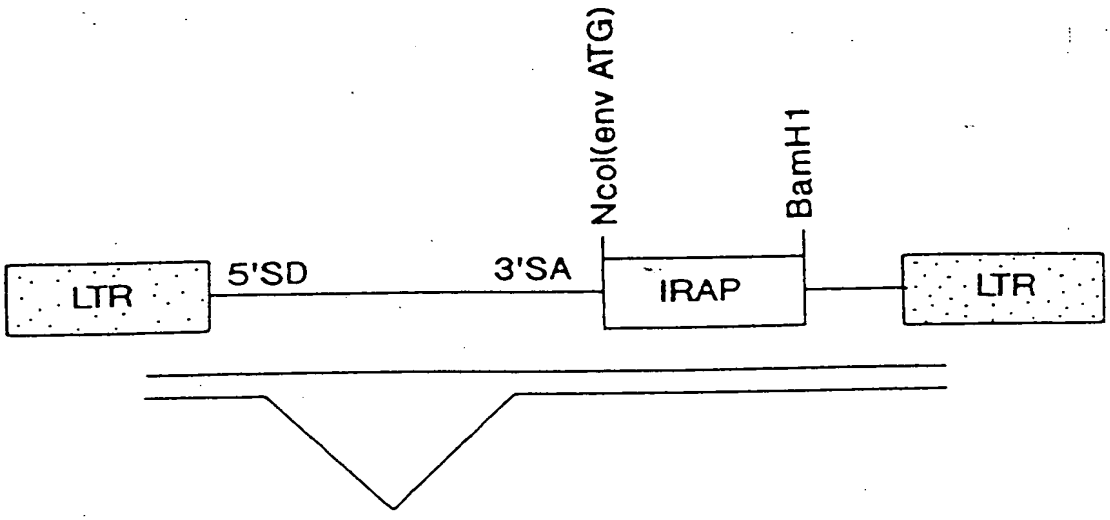

NcoI(env ATG)
BamH1
LTR
5'SD
3'SA
IRAP
LTR

FIG. 1

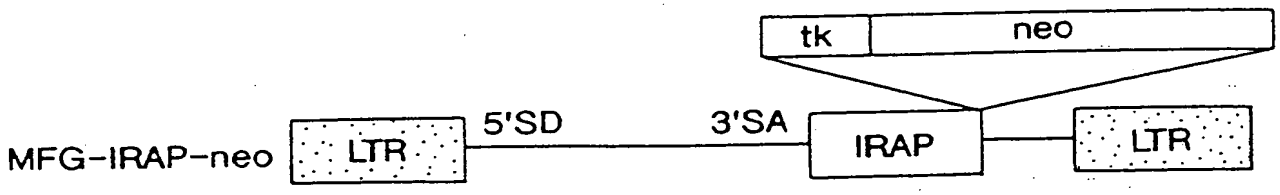

tk
neo
MFG-IRAP-neo
LTR
5'SD
3'SA
IRAP
LTR

FIG. 2

FIG. 3

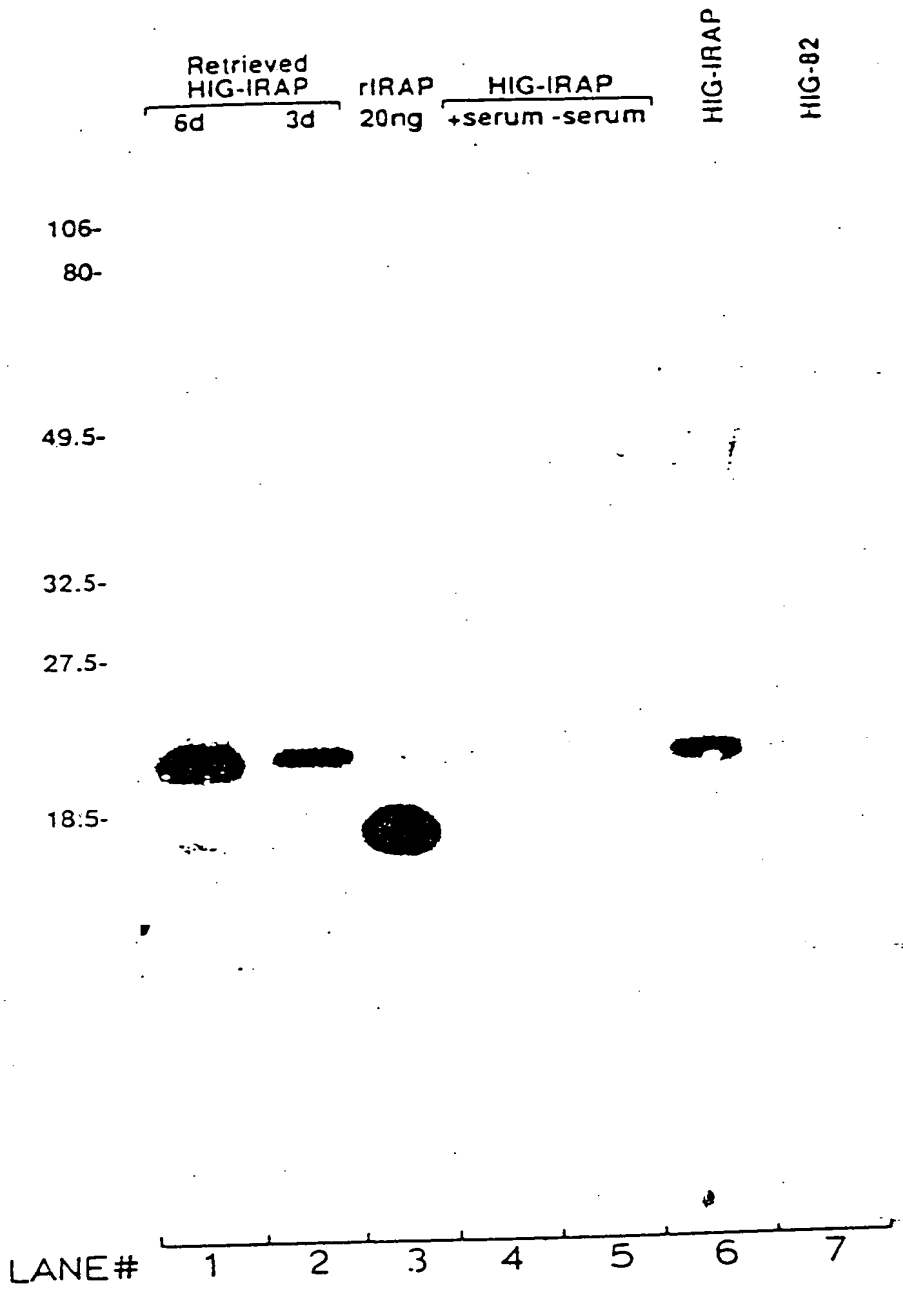

Retrieved HIG-IRAP
6d
3d
rIRAP 20ng
HIG-IRAP
+serum
-serum
HIG-IRAP
HIG-82
106-
80-
49.5-
32.5-
27.5-
18.5-
LANE#
1
2
3
4
5
6
7

FIG. 4

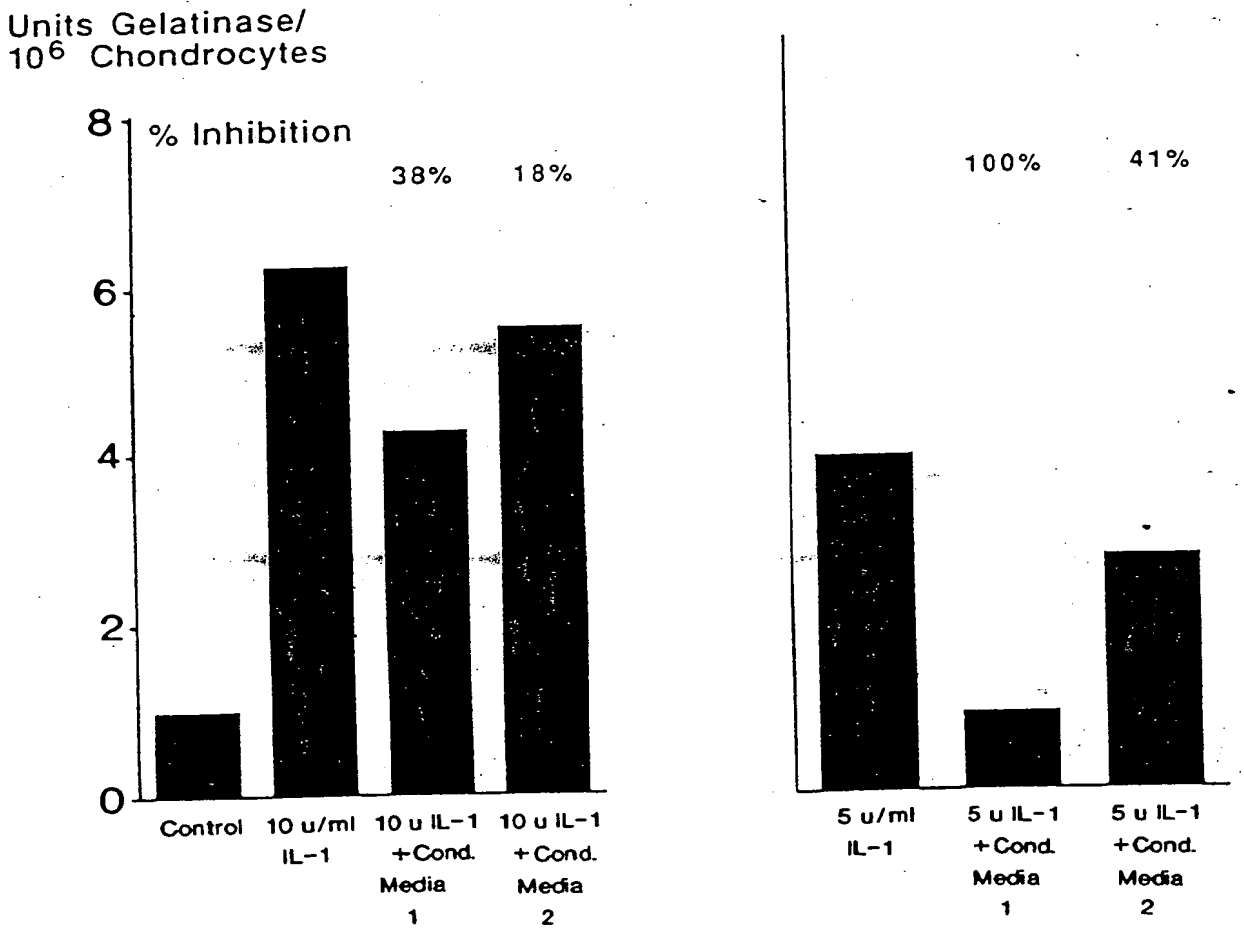

Units Gelatinase/
10^6 Chondrocytes
8
6
4
2
0
% Inhibition
38%
18%
100%
41%
Control
10 u/ml IL-1
10 u IL-1 +Cond. Media 1
10 u IL-1 +Cond. Media 2
5 u/ml IL-1
5 u IL-1 +Cond. Media 1
5 u IL-1 +Cond. Media 2

FIG. 5

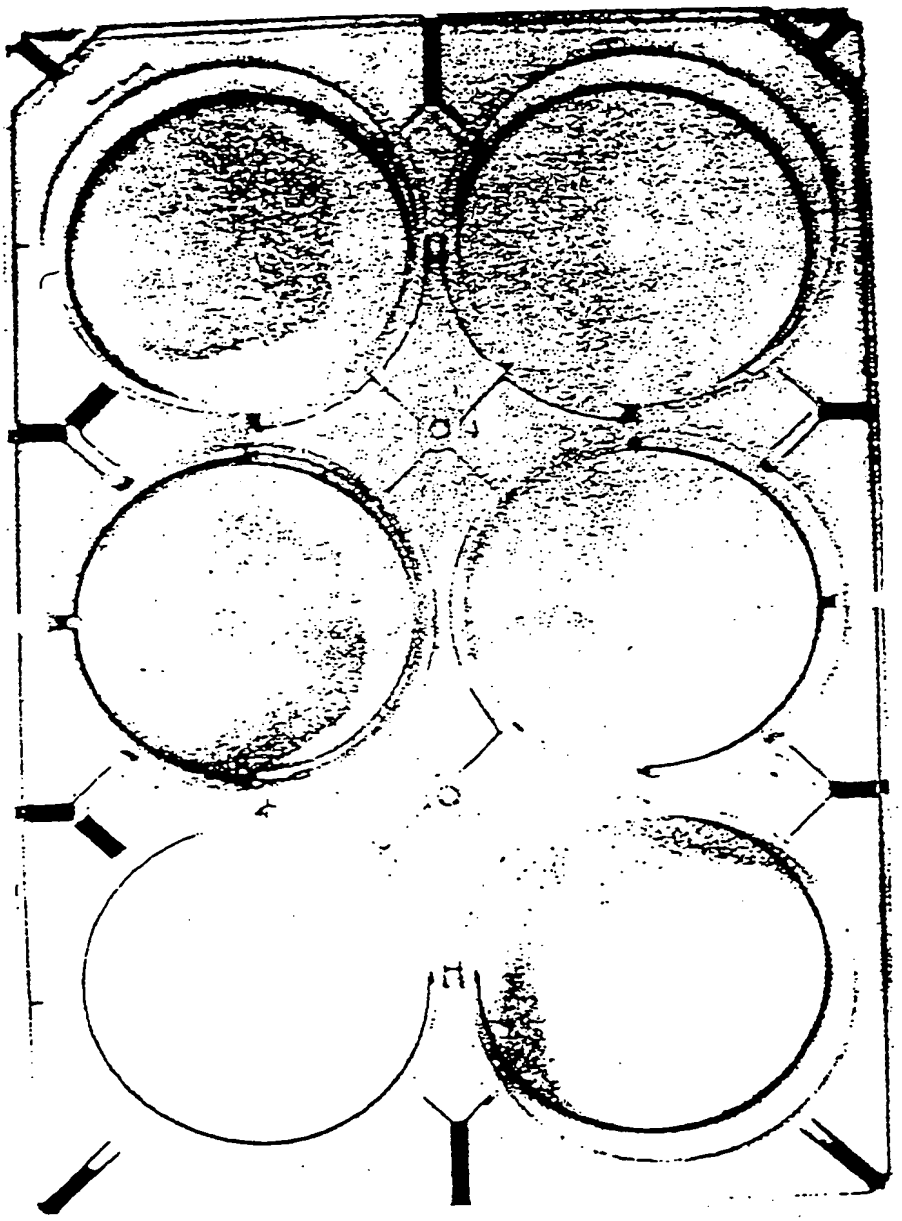


FIG. 6

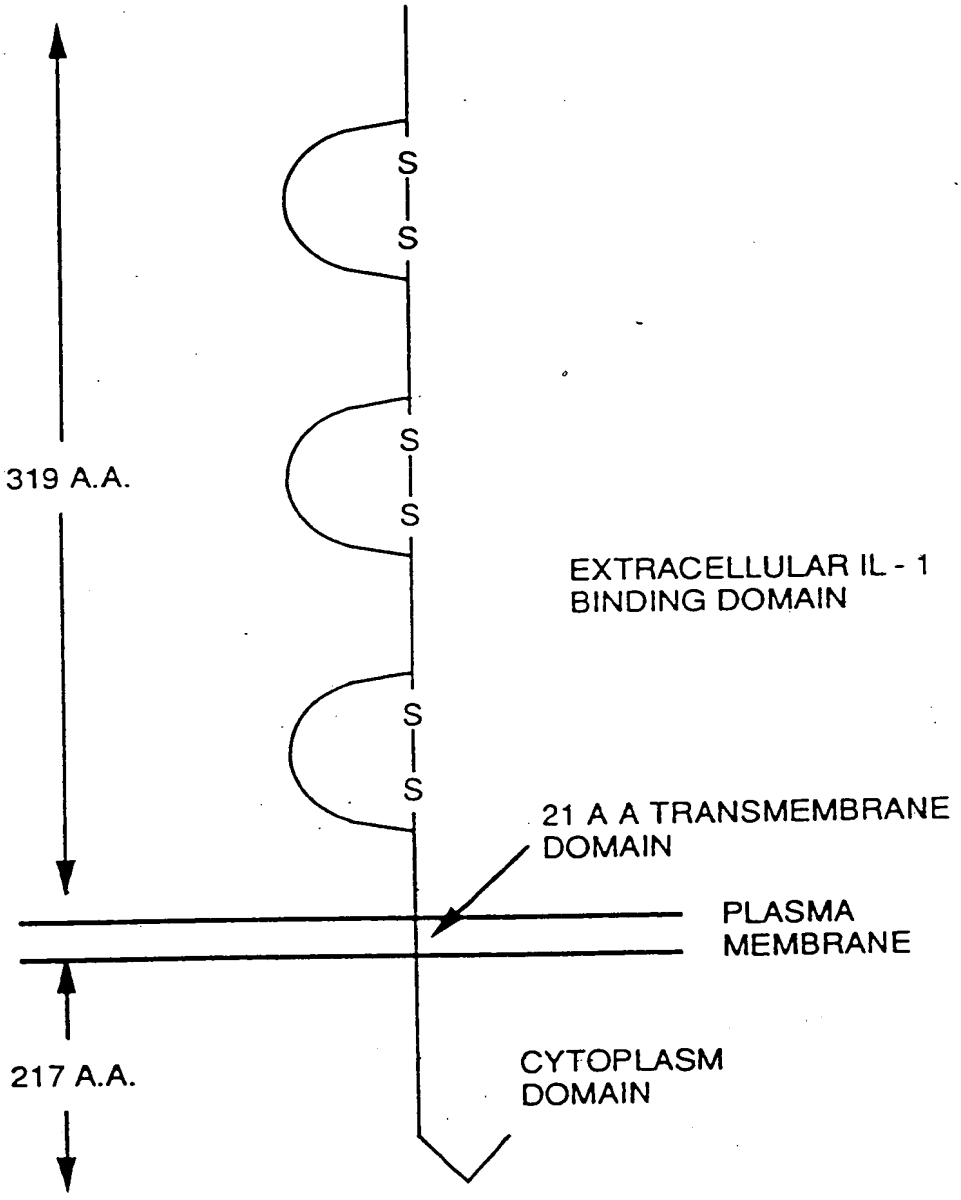

S
S
S
S
S
S
319 A.A.
EXTRACELLULAR IL - 1
BINDING DOMAIN
21 A A TRANSMEMBRANE
DOMAIN
PLASMA
MEMBRANE
217 A.A.
CYTOPLASM
DOMAIN

FIG. 7

FIG. 8A

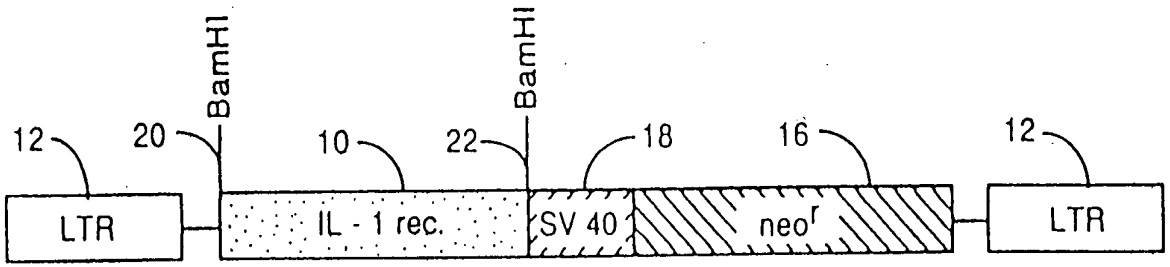

H ValIleValSerProAlaAsnGluThrMetGluValAspLeuGlySerGlnIleGlnLeuIleCysAsnValThrGlyGlnLeuSerAspIleAlaTyrTrpLys 244
H GTGATTGTGAGCCCAGCTAATGAGACAATGGAAGTAGACTTGGGATCCCAGATACAATTGATCTGTAATGTCACCGGCCAGTTGAGTGACATTGCTTACTGGAAG 732
M GTTATCCTGAGCCCTCGGAATGAGACGATCGAAGCTGACCCAGGATCAATGATACAACTGATCTGCAACGTCACGGGCCAGTTCTCAGACCTTGTCTACTGGAAG 735
M ******Leu******Arg*********Ile***Ala***Pro******Met**********Phe******LeuVal******** 245
H TrpAsnGlySerValIleAspGluAspAspProValLeuGlyGluAspTyrTyrSerValGluAsnProAlaAsnLysArgArgSerThrLeuIleThrValLeu 273
H TGGAATGGGTCAGTAATTGATGAAGATGACCCAGTGCTAGGGGAAGACTATTACAGTGTGGAAAATCCTGCAAACAAAACAAGGAGTACCCTCATCACAGTGCTT 137
M TGGAATGGATCAGAAATTGAATGGAATGATCCATTTCTAGCTGAAGACTATCAATTTGTGGAACATCCTTCAACCAAAAGAAAATACACACTCATTACAACACTT 140
M ************Glu***GluTrpAsn******Phe***Ala*********GlnPhe******His***SerThr******LysTyr***********Thr*** 250
H AsnIleSerGluIleGluSerArgPheTyrLysHisProPheThrCysPheAlaLysAsnThrHisGlyIleAspAlaAlaTyrIleGlnLeuIleTyrProVal 314
H AATATATCGGAAATTGAAAGTAGATTTTATAAACATCCATTTACCTGTTTTGCCAAGAATACACATGGTATAGATGCAGCATATATCCAGTTAATATATCCAGTC 942
M AACATTTCAGAAGTTAAAAGCCAGTTTTATCGCTATCCGTTTATCTGTGTTGTTAAGAACACAAATATTTTTGAGTCGGCGCATGTGCAGTTAATATACCCAGTC 945
M ************ValLys***Gln******ArgTyr******Ile***ValVal*********AsnIlePheGluSer***HisVal********** 315
3'
H ThrAsnPheGlnLysHisMetIleGlyIleCysValThrLeuThrValIleIleValCysSerValPheIleTyrLysIlePheLysIleAspIleValLeuTrp 349
H ACTAATTTCCAGAAGCACATGATTGGTATATGTGTCACGTTGACAGTCATAATTGTGTGTTCTGTTTTCATCTATAAAATCTTCAAGATTGACATTGTGCTTTGG 1047
M CCTGACTTCAAGAATTACCTCATCGGGGGCTTTATCATCCTCACGGCTACAATTGTATGCTGTGTGTGCATCTATAAAGTCTTCAAGGTTGACATAGTGCTTTGG 1050
M ProAsp***LysAsnTyrLeu******GlyPheIleIle******AlaThr*********Cys***Cys*********Val******Val********** 350
H TyrArgAspSerCysTyrAspPheLeuProIleLysAlaSerAspGlyLysThrTyrAspAlaTyrIleLeuTyrProLysThrValGlyGluGlySerThrSer 354
H TACAGGGATTCCTGCTATGATTTTCTCCCAATAAAAGCTTCAGATGGAAAGACCTATGACGCATATATACTGTATCCAAAGACTGTTGGGGAAGGGTCTACCTCT 1152
M TACAGGGACTCCTGCTCTGGTTTTCTTCCTTCAAAAGCTTCAGATGGAAAGACATACGATGCCTATATTCTTTATCCCAAGACCCTGGGAGAGGGGTCCTTCTCA 1155
M **************SerGly*********Ser**Leu***********Phe*** 385
H AspCysAspIlePheValPheLysValLeuProGluValLeuGluLysGlnCysGlyTyrLysLeuPheIleTyrGlyArgAspAspTyrValGlyGluAspIle 419
H GACTGTGATATTTTTGTGTTTAAAGTCTTGCCTGACGTCTTGGAAAAACAGTGTGGATATAAGCTGTTCATTTATGGAAGGGATGACTACGTTGGGGAAGACATT 1257
M GACTTAGATACTTTTGTTTTTAAACTGTTGCCTGACGTCTTGGAGGGACAGTTTGGATACAAGCTGTTCATTTATGGAAGGGATGACTATGTTGGAGAAGATACC 1260
M ***Leu***Thr***********Leu*****************Gly***Phe**Thr 420

FIG. 8B


H ValGluValIleAsnGluAsnValLysLysSerArgArgLeuIleIleIleLeuValArgGluThrSerGlyPheSerTrpLeuGlyGlySerSerGluGluGln 454
H GTTGAGGTCATTAATGAAAACGTAAAGAAAAGCAGAAGACTGATTATCATTTTAGTCAGAGAAACATCAGGCTTCAGCTGGCTGGGTGGTTCATCTGAAGAGCAA 1362
M ATCGAGGTTACTAATGAAAATGTAAAGAAAAGCAGGAGGCTGATTATCATTCTAGTGAGAGATATGGCAGGCTTCAGCTGGCTGGCCCAGTCATCTGAAGAGCAA 1353
M Ile******Thr*****AspMetGly*****Gln***** 455
H IleAlaMetTyrAsnAlaLeuValGlnAspGlyIleLysValValLeuLeuGluLeuGluLysIleGlnAspTyrGluLysMetProGluSerIleLysPheIle 489
H ATAGCCATGTATAATGCTCTTGTTCAGGATGGAATTAAAGTTGTCCTGCTTGAGCTGGAGAAAATCCAAGACTATGAGAAAATGCCAGAATCGATTAAATTCATT 1467
M ATAGCCATATACAATGCTCTCATCCAGGAAGGAATTAAAATCGTCCTGCTTGAGTTGGAGAAAATCCAAGACTATGAGAAAATGCCAGATTCTATTCAGTTCATT 1470
M ******Ile**********Ile***Glu********Ile*****Asp******Gln****** 490
H LysGlnLysHisGlyAlaIleArgTrpSerGlyAspPheThrGlnGlyProGlnSerAlaLysThrArgPheTrpLysAsnValArgTyrHisMetProValGln 524
H AAGCAGAAACATGGGGCTATCCGCTGGTCAGGGGACTTTACACAGGGACCACAGTCTGCAAAGACAAGGTTCTGGAAGAATGTCAGGTACCACATGCCAGTCCAG 1572
M AAGCAGAAACACGGAGTCATTTGCTGGTCAGGAGACTTTCAAGAAAGACCACAGTCTGCAAAGACCAGGTTCTGGAAAAACTTAAGATACCACATGCCAGCCCAA 1575
M **********Val***Cys**********GlnGluArg*****Leu******Gln******Ala*** 525
H ArgArgSerProSerSerLysHisGlnLeuLeuSer----------ProAlaThrLysGluLysLeuGlnArgGluAlaHisValProLeuGlyEnd 552
H CGACCGTCACCTTCATCTAAACACCAGTTACTGTC----------ACCAGCCACTAAGGAGAAACTGCAAAGAGAGGCTCACGTGCCTCTCGCGTAGCATGGA 1665
M CGGAGATCACCATTGTCTAAACACCGCTTACTAACCCTGGATCCTGTGCGGGACACTAAGGAGAAACTGCCGGCAGCAACACACTTACCACTCGGCTAGCATGGC 1680
M **********Leu*********Arg******ThrLeuAspProValArgAsp**********ProAlaAlaThr********** 557

FIG. 8C

Structure Of The PLJ - ILrec Retroviral Vector
And Partial Restriction Endonuclease Map



LTR - Long Terminal Repeats - Regulates Viral Transcription And Expression Of IL - 1 Receptor

neo^r - Bacterial Gene Encoding Resistance To The Antibiotic Neomycin

SV 40 - Simian Virus 40 Enhancer Promoter - Regulates Expression Of The neo^r Gene

FIG. 9

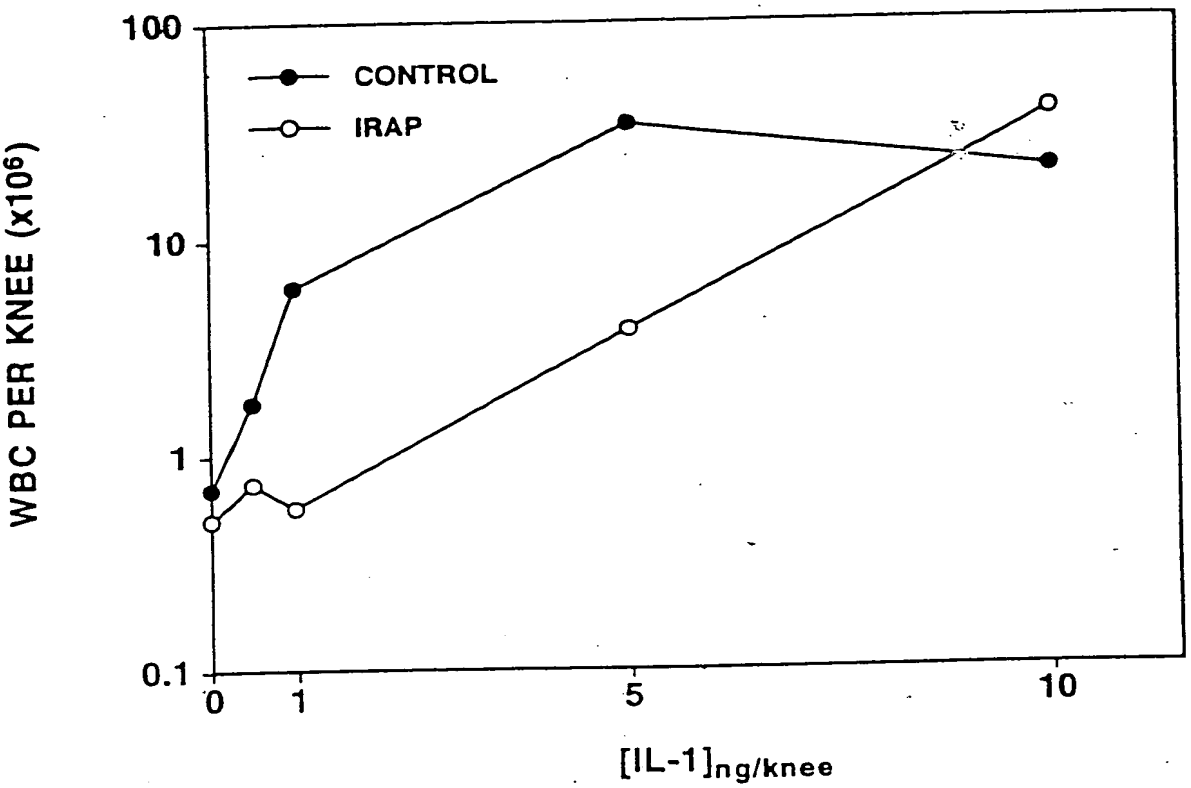

100
10
1
0.1
CONTROL
IRAP
WBC PER KNEE (x10⁶)
0
1
5
10
[IL-1]ng/knee

FIG. 10

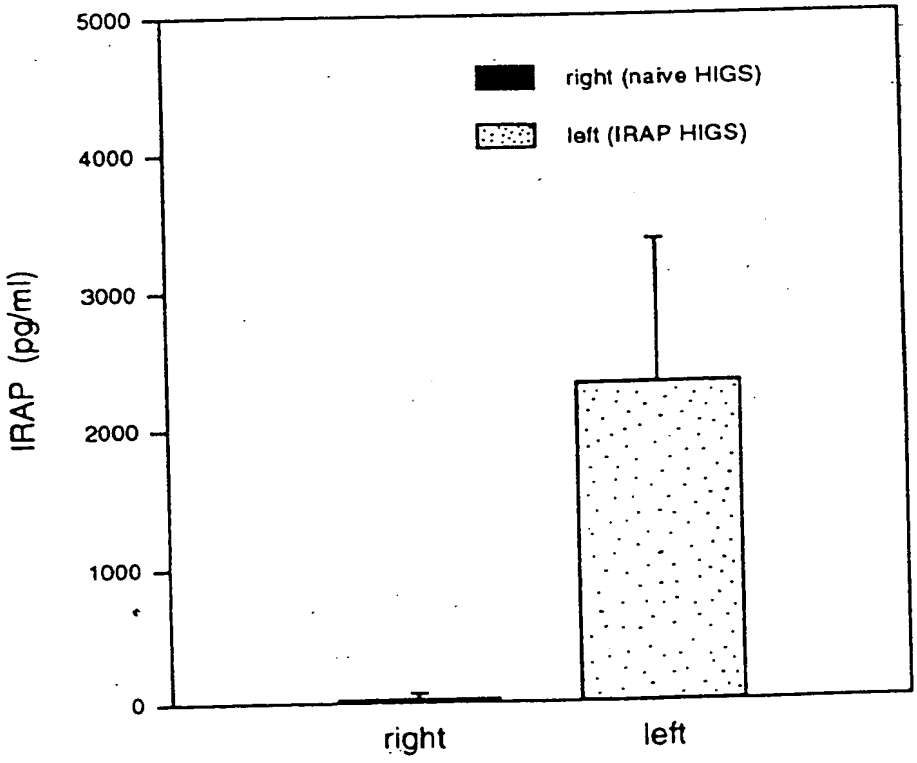

5000
4000
3000
2000
1000
0
right (naive HIGS)
left (IRAP HIGS)
IRAP (pg/ml)
right
left

FIG. 11

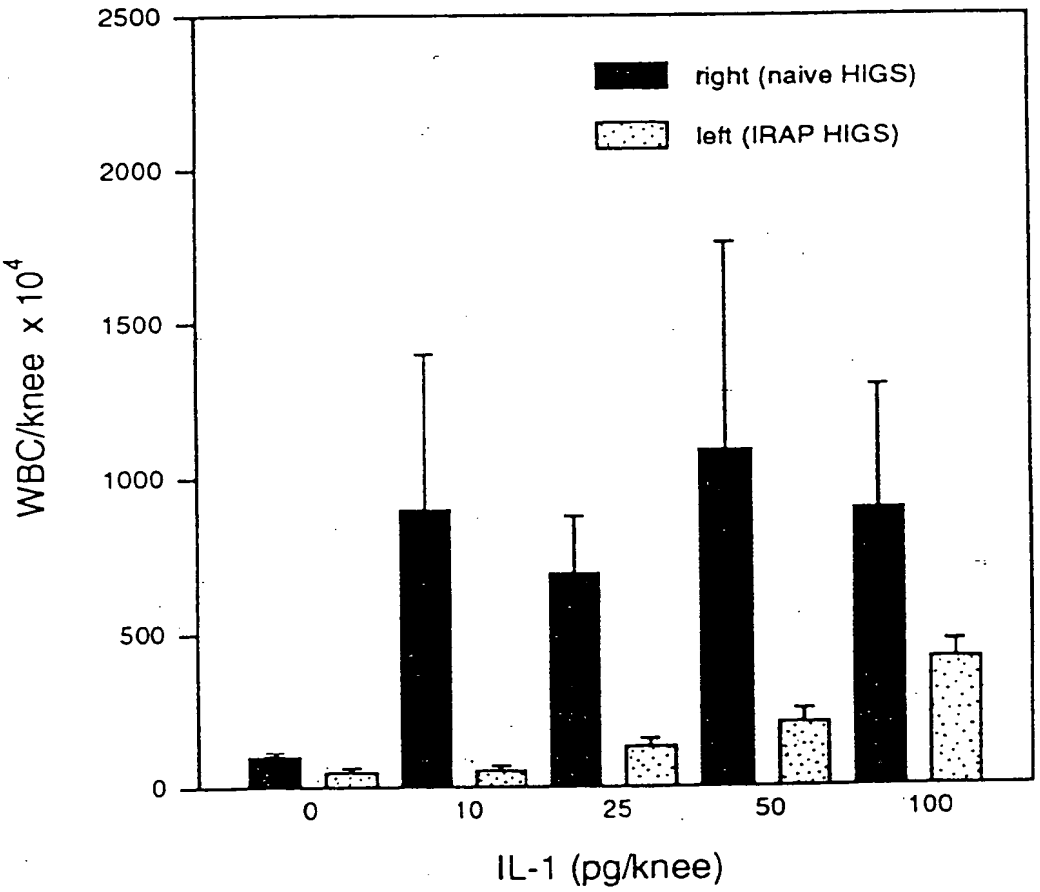

2500
2000
1500
1000
500
0
WBC/knee x 10^4
right (naive HIGS)
left (IRAP HIGS)
0
10
25
50
100
IL-1 (pg/knee)

FIG. 12A

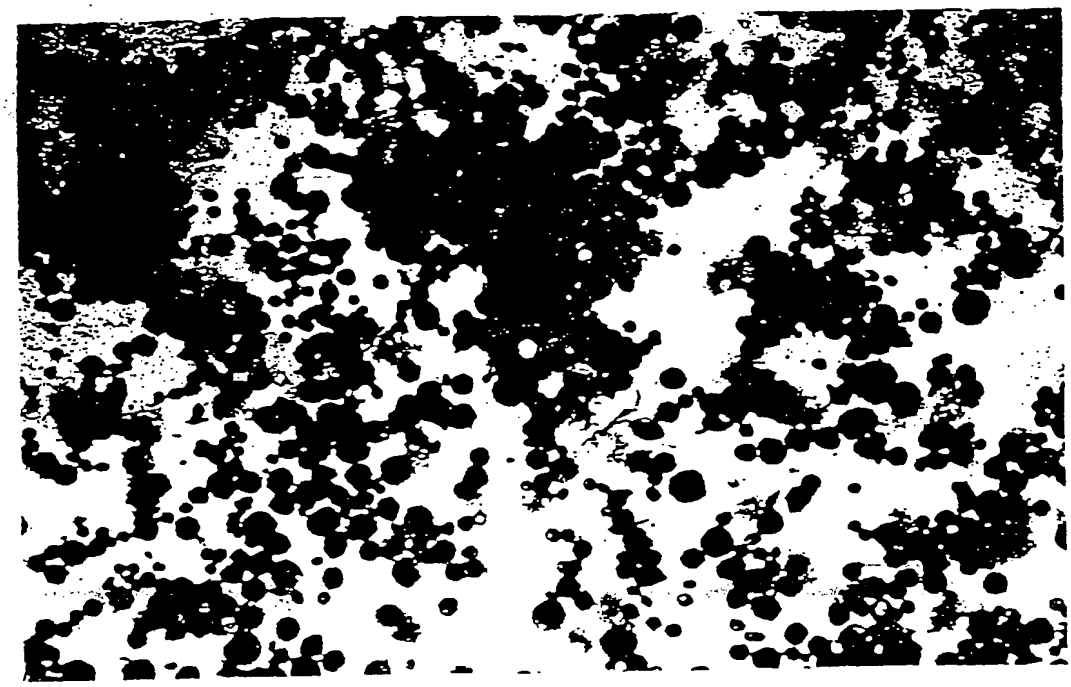


FIG. 12B

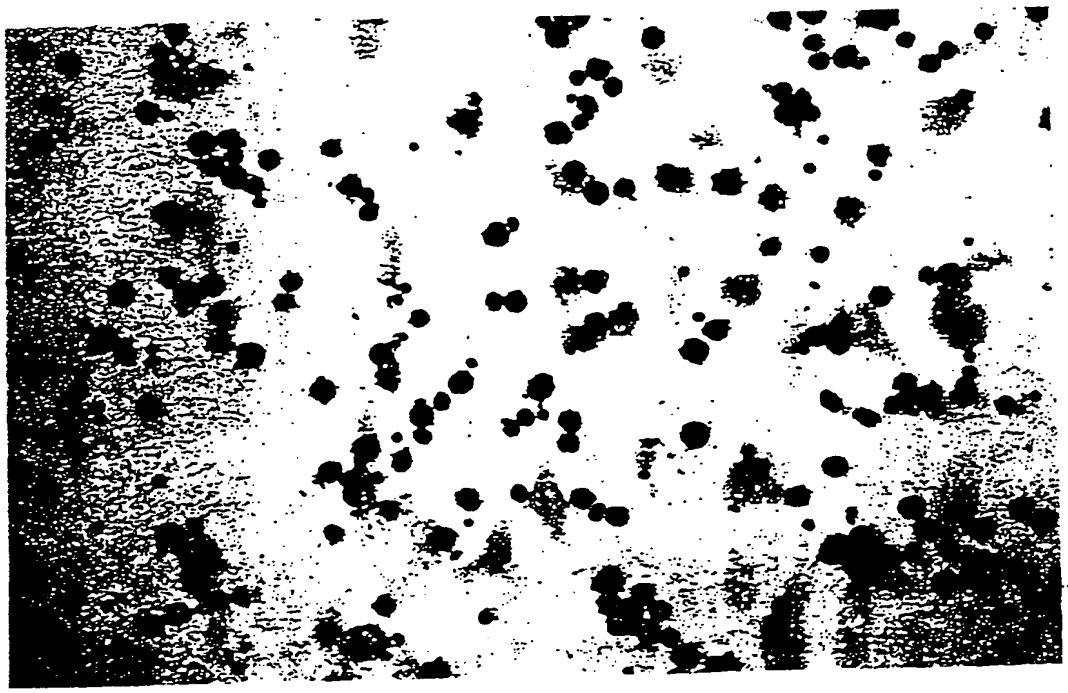


FIG. 12C

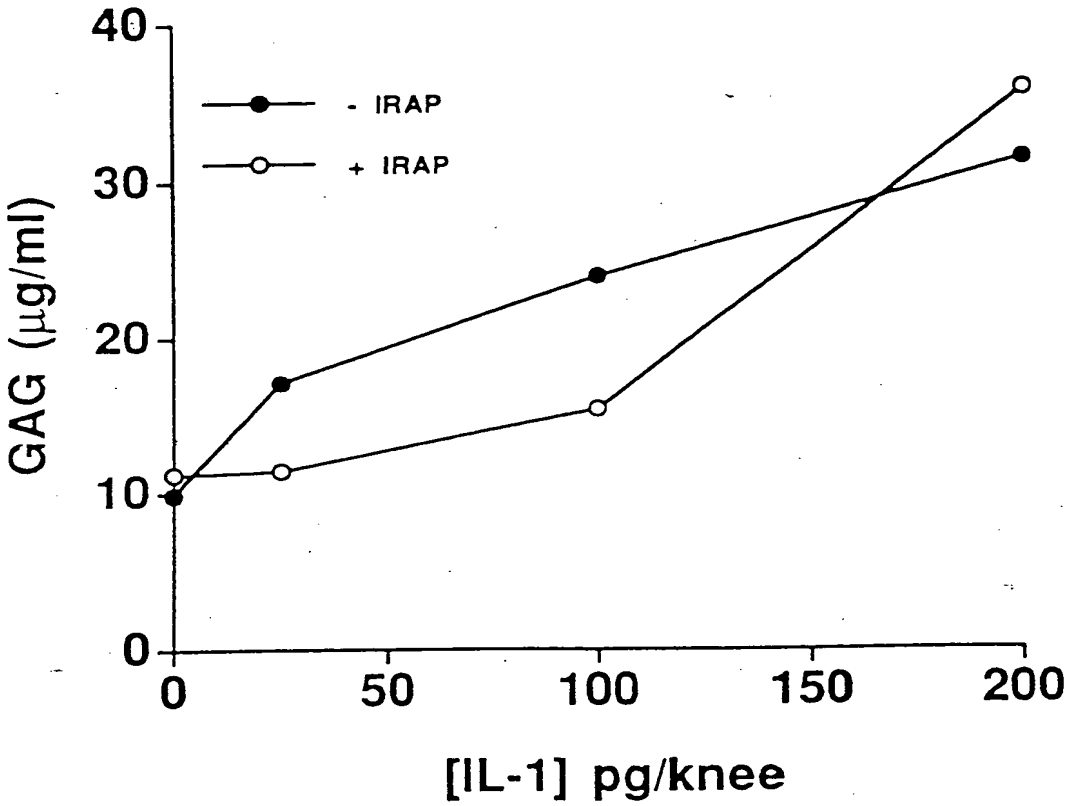


FIG. 13

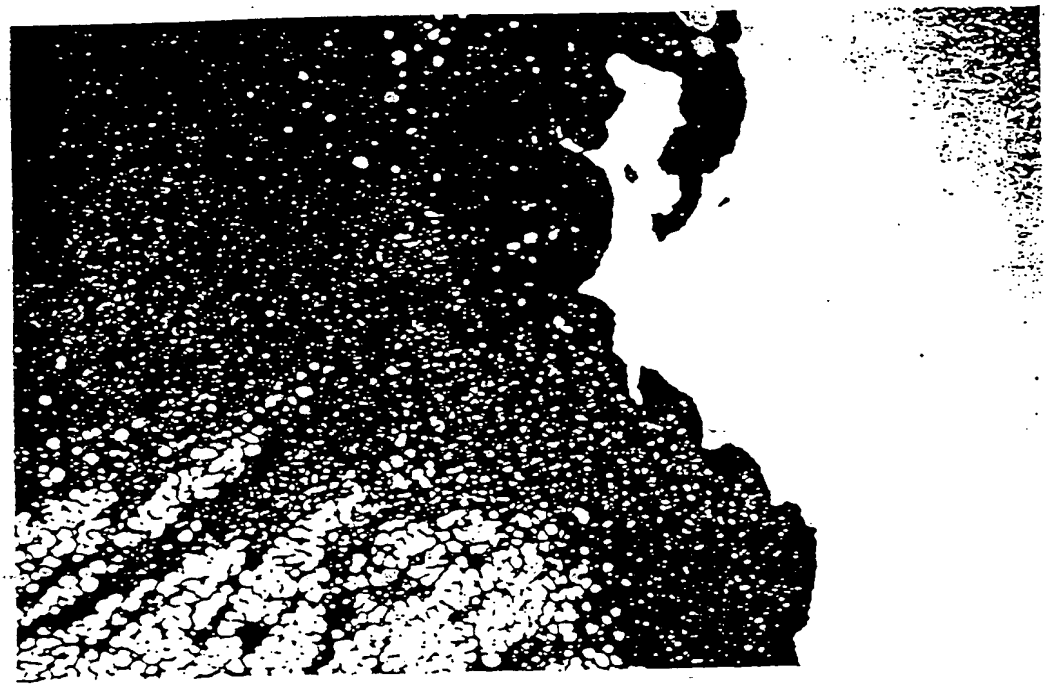


FIG. 14A

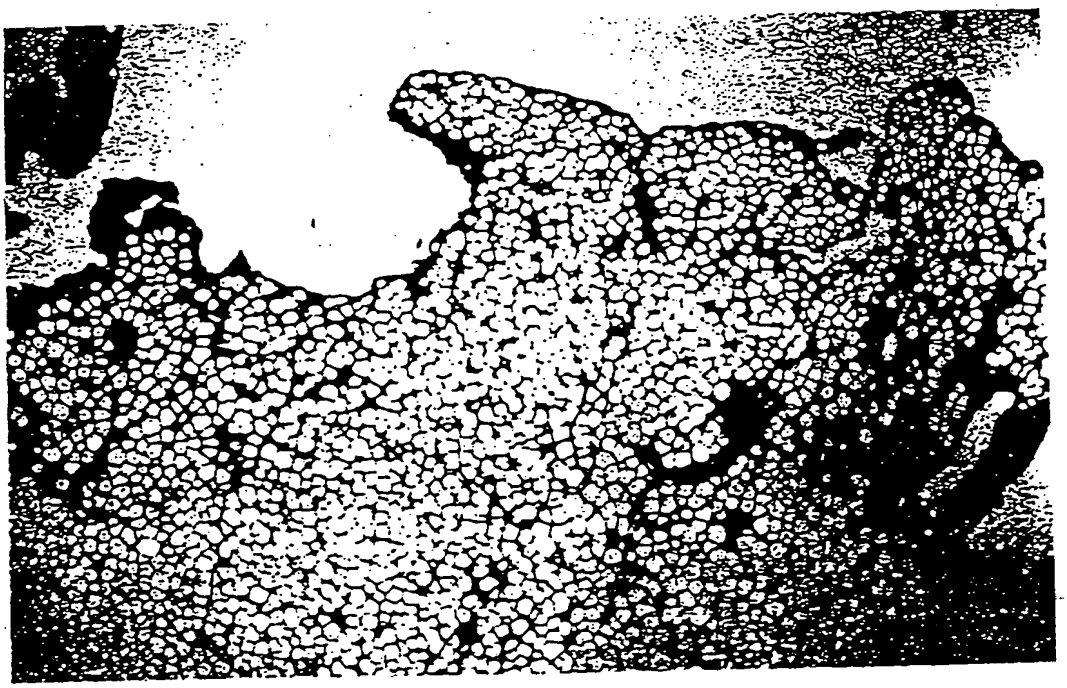


FIG. 14B

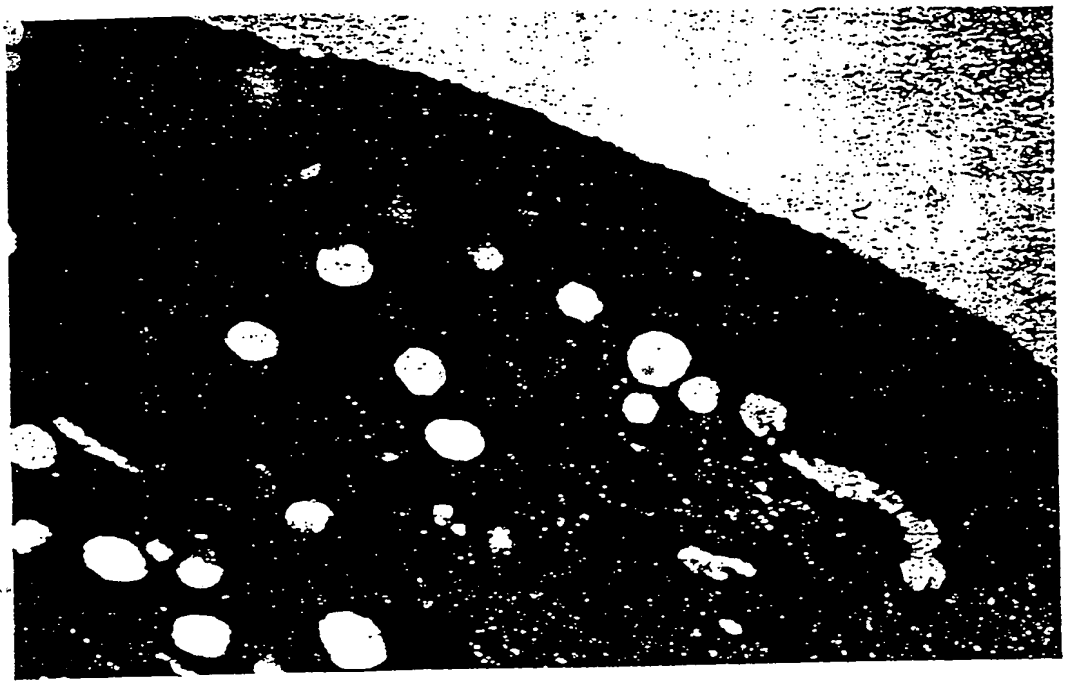


FIG. 14C

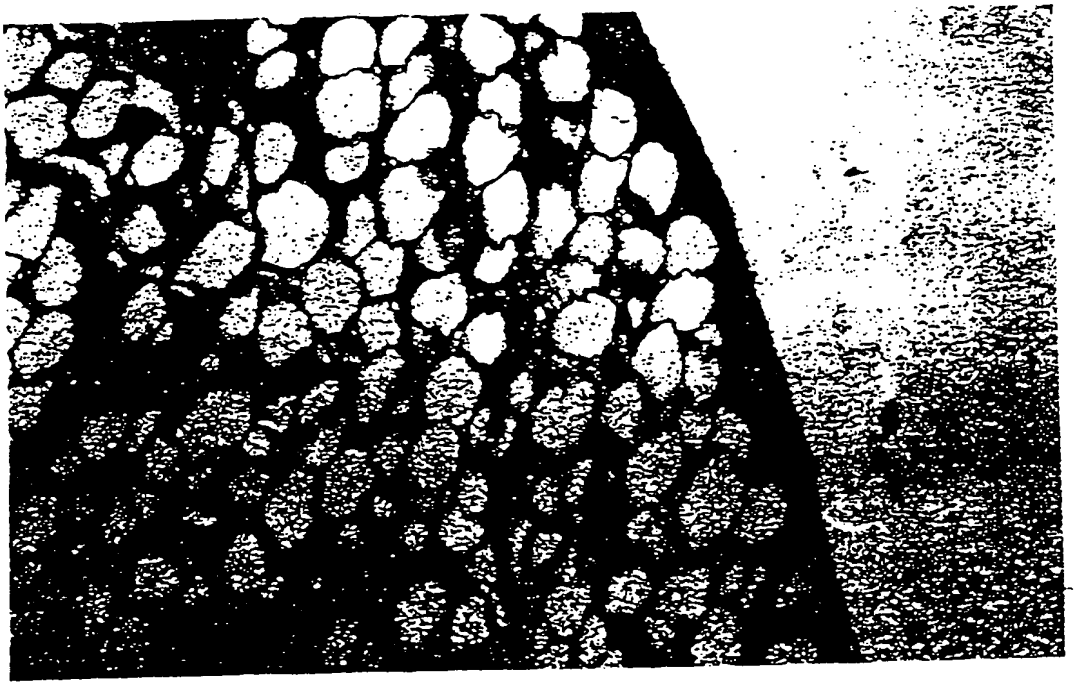


FIG. 14D

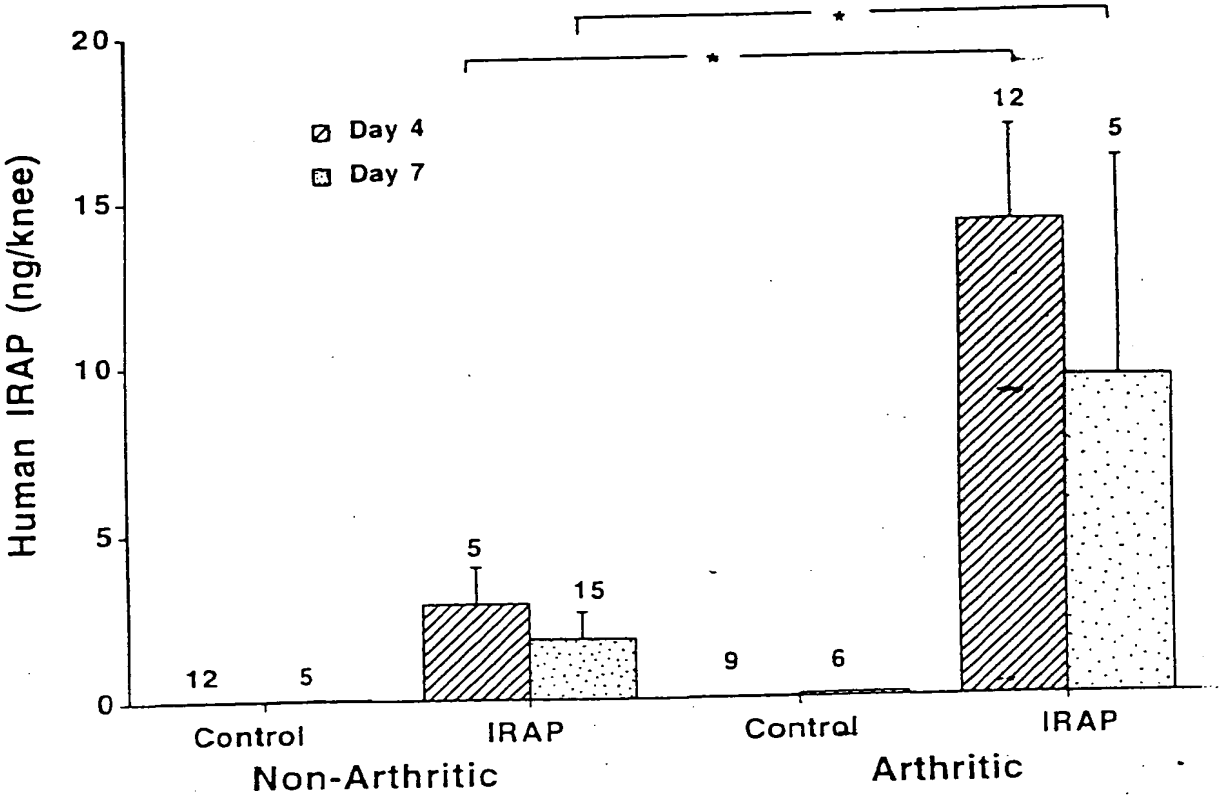

Human IRAP (ng/knee)
20
15
10
5
0
Day 4
Day 7
*
*
12
5
5
15
9
6
12
5
Control
IRAP
Control
IRAP
Non-Arthritic
Arthritic

FIG. 15

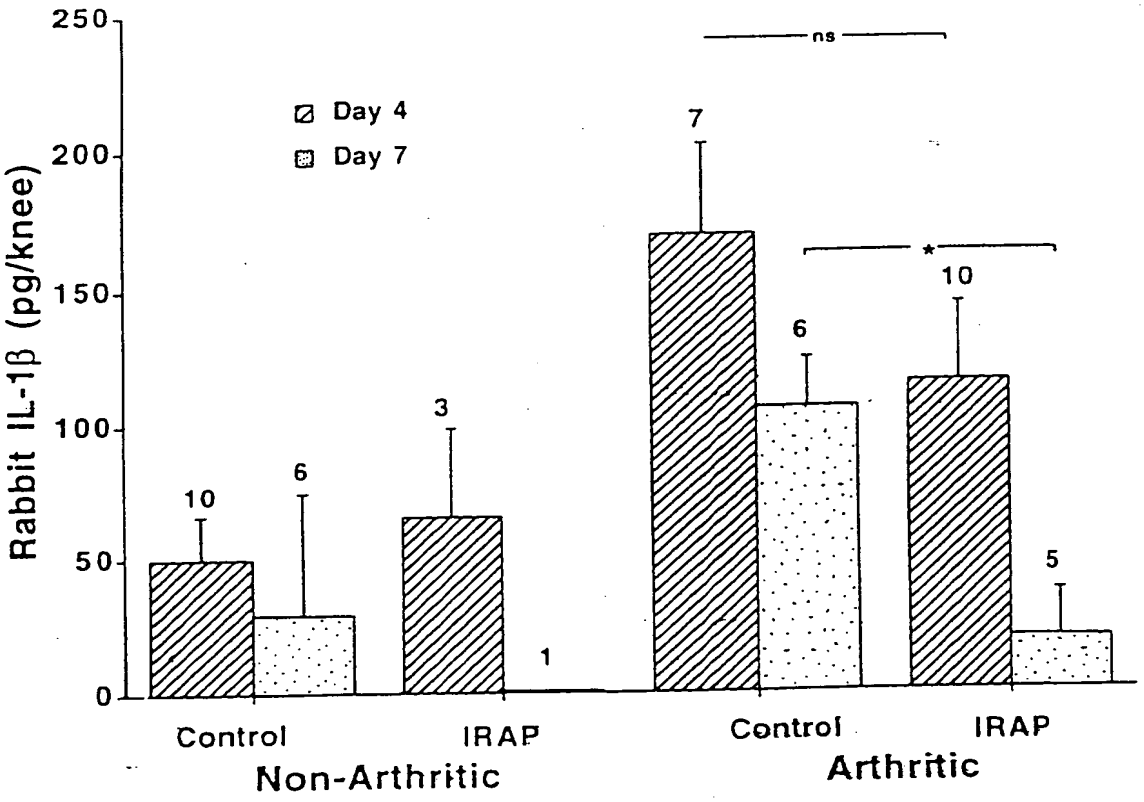

Rabbit IL-1β (pg/knee)
250
200
150
100
50
0
Day 4
Day 7
ns
*
10
6
3
1
7
6
10
5
Control
IRAP
Control
IRAP
Non-Arthritic
Arthritic

FIG. 16

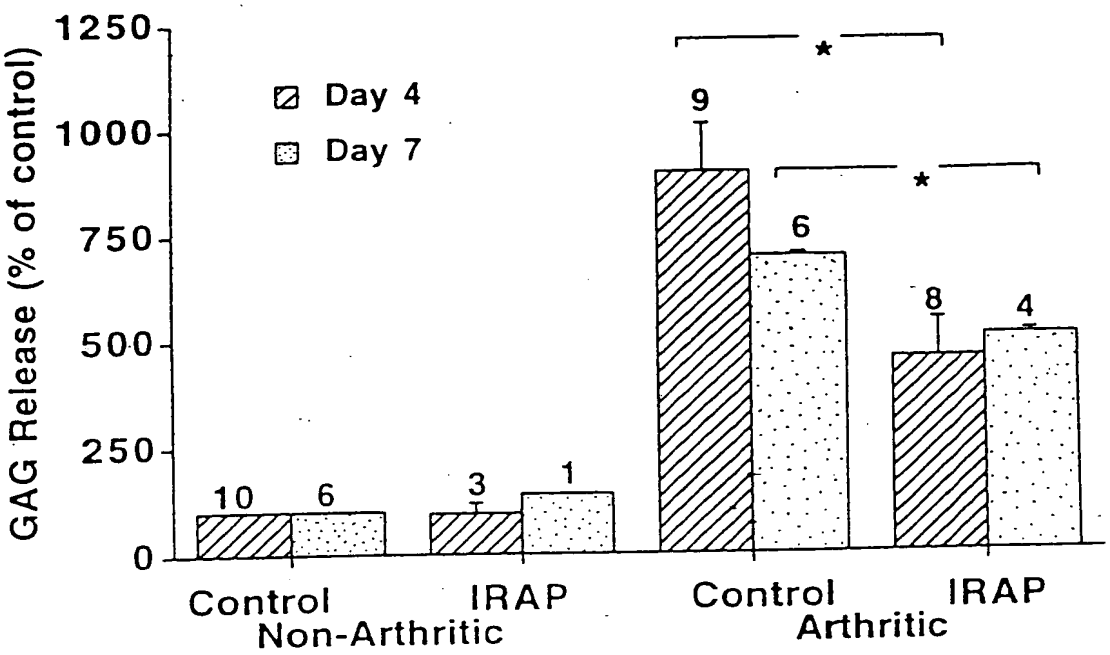


FIG. 17A

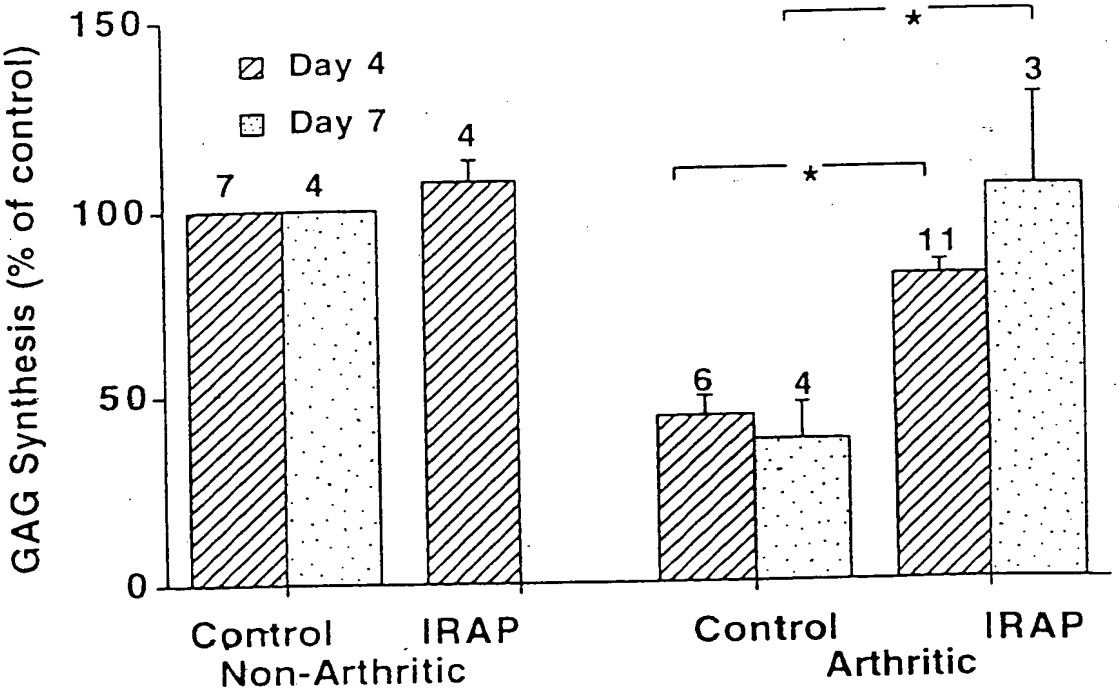


FIG. 17B

09207 5275250

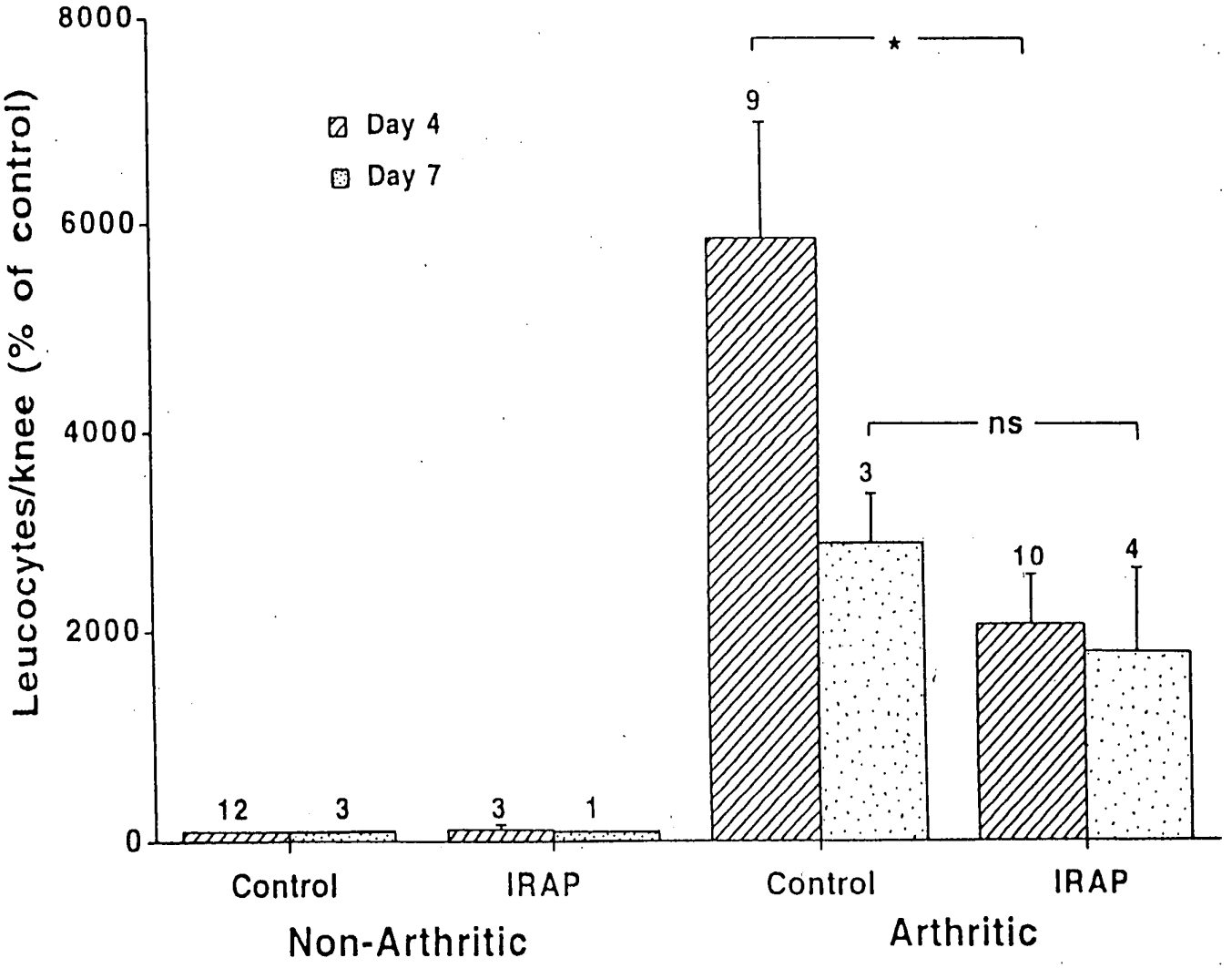


FIG. 18

SUBSTITUTE SHEET

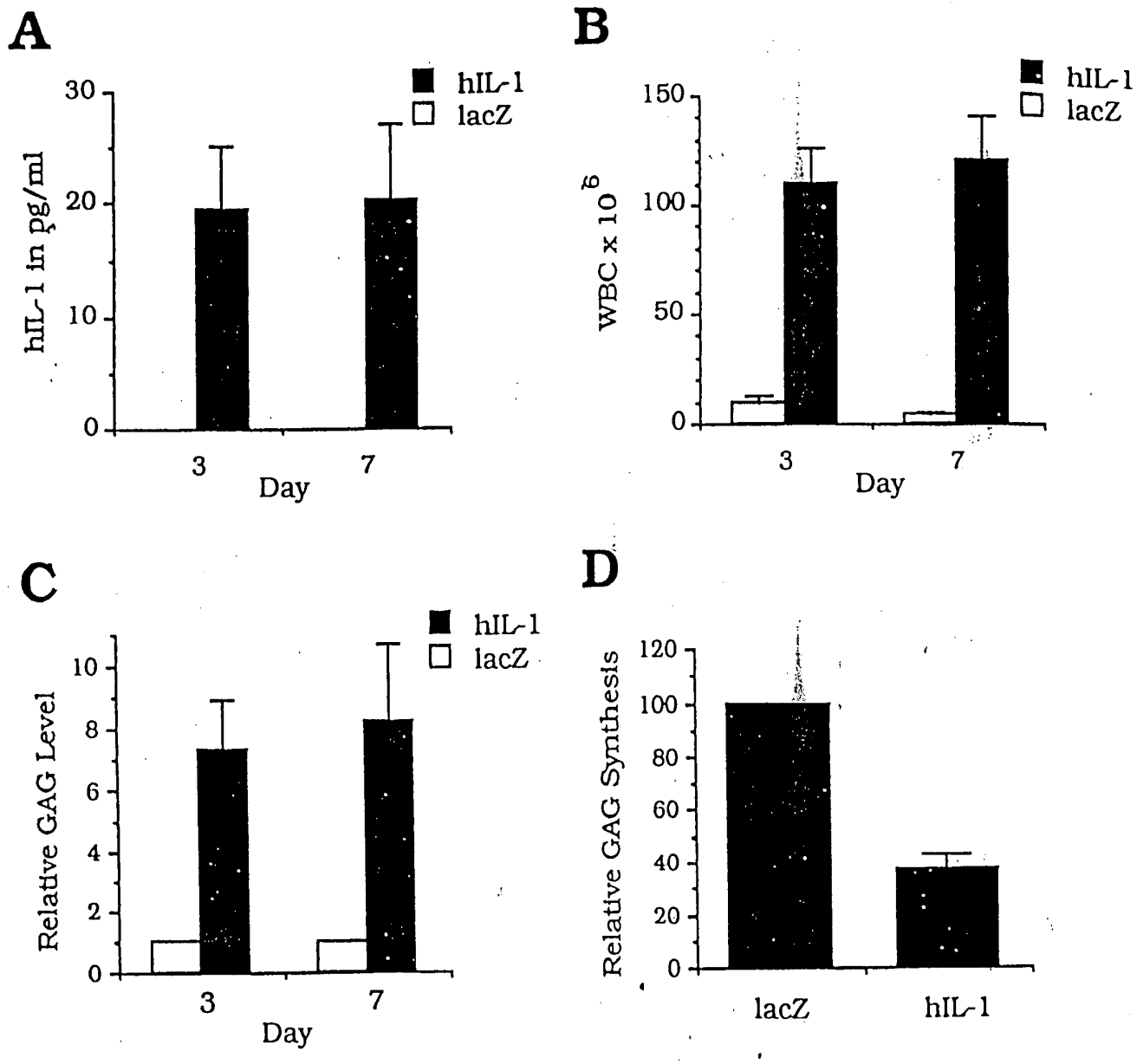


FIG. 19.

SUBSTITUTE SHEET (RULE 26)

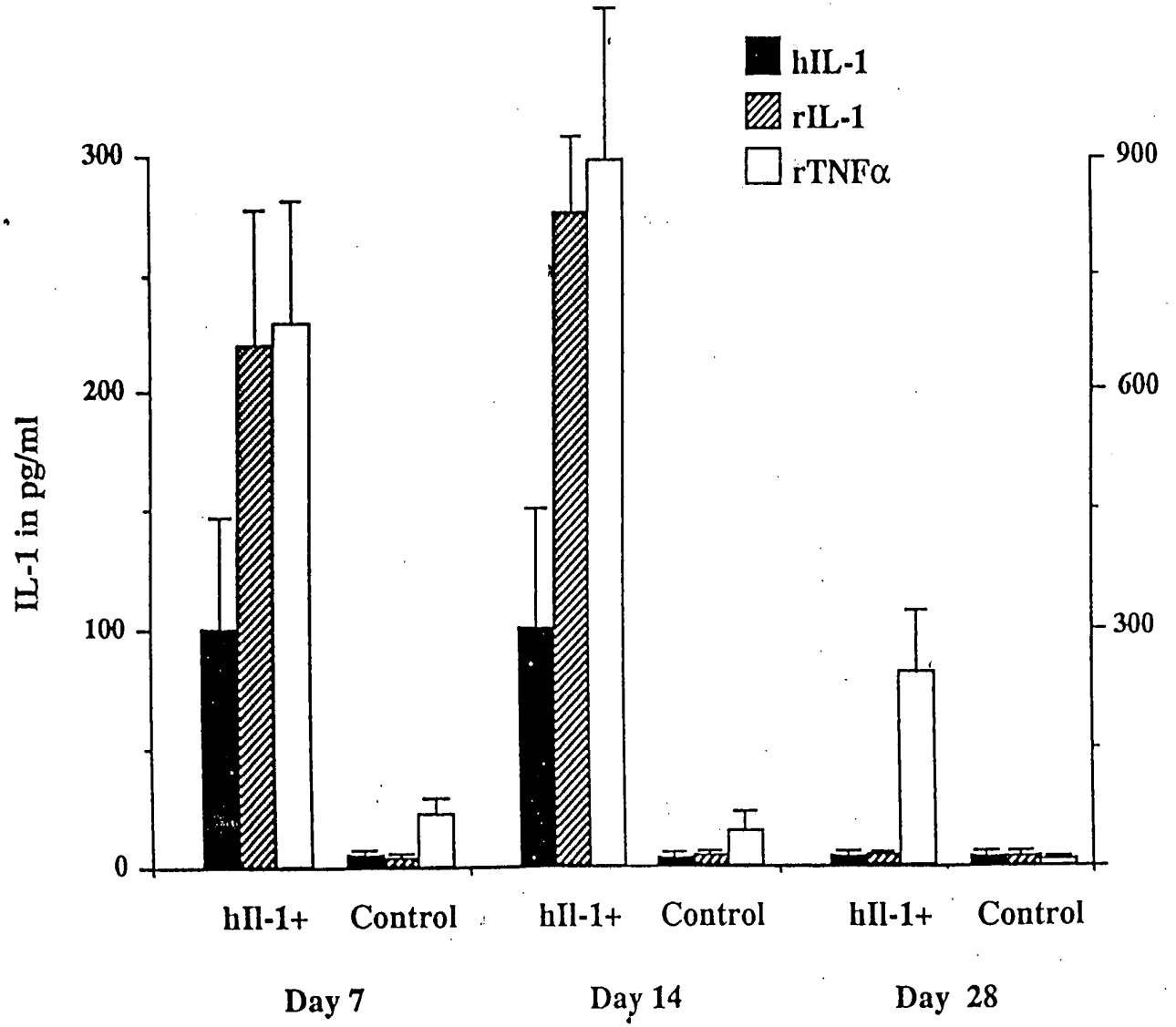


FIG. 20.

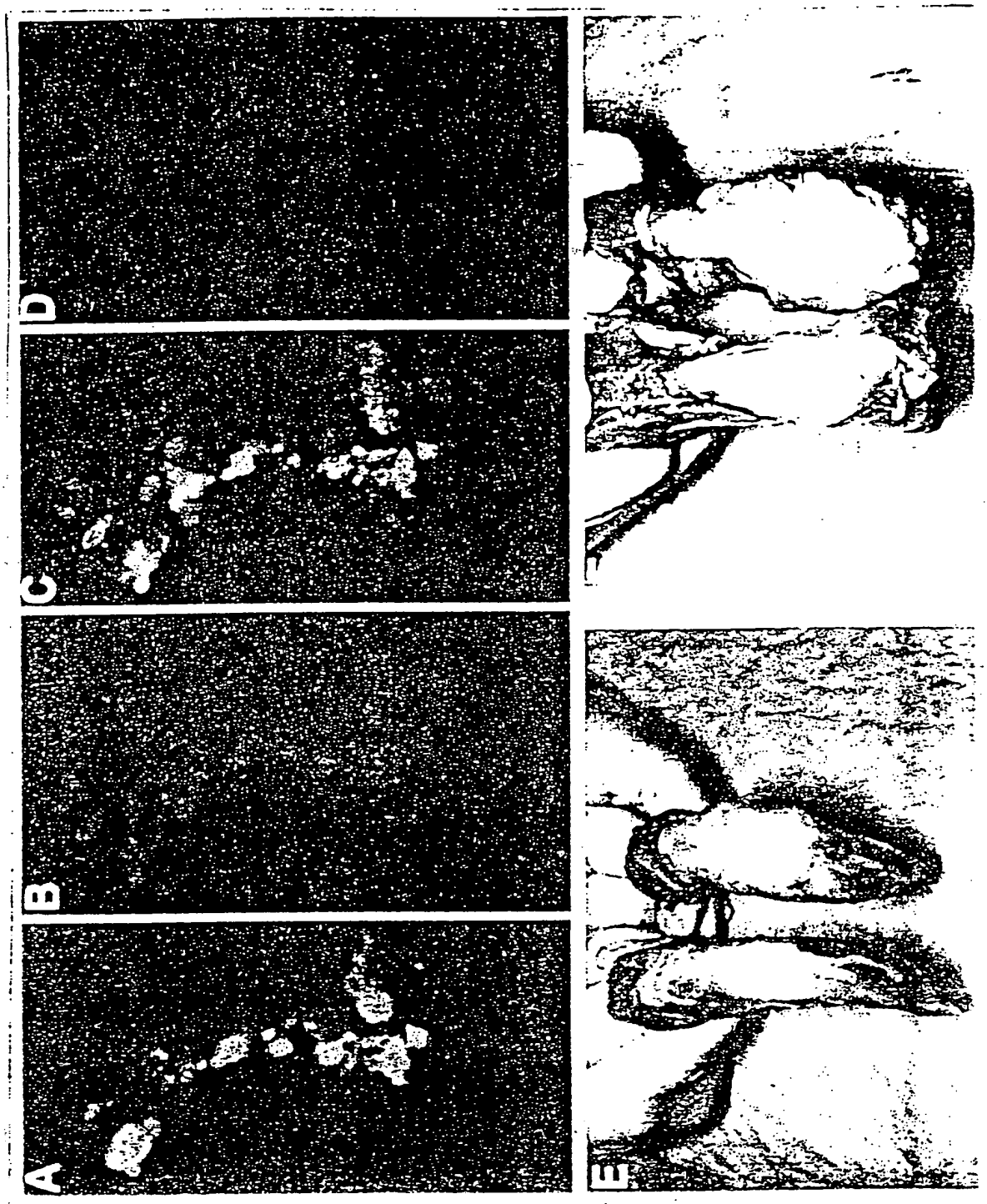


FIG. 21.

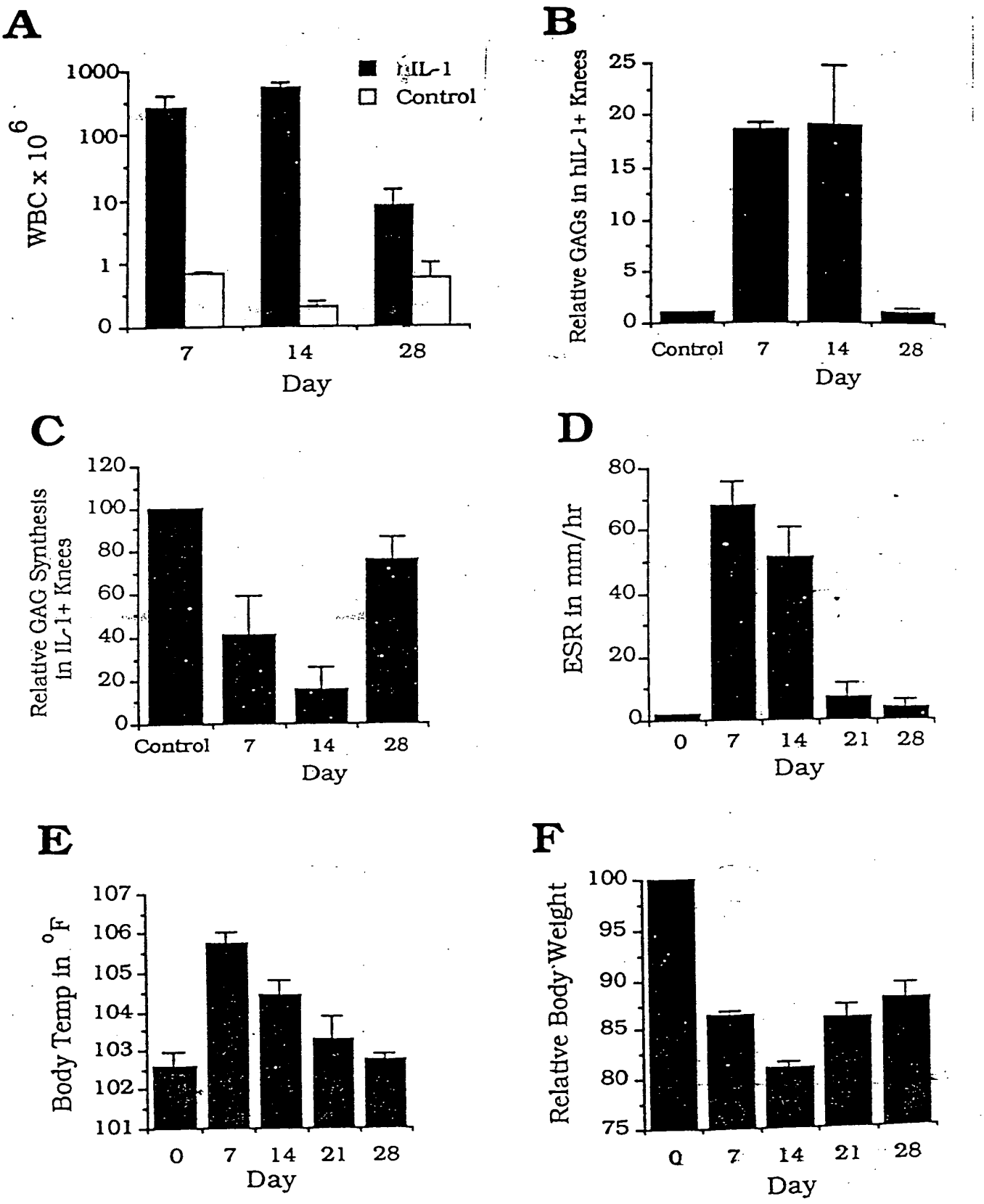

A
WBC x 10^6
1000
100
10
1
0
hIL-1
Control
7
14
28
Day
B
Relative GAGs in hIL-1+ Knees
25
20
15
10
5
0
Control
7
14
28
Day
C
Relative GAG Synthesis in IL-1+ Knees
120
100
80
60
40
20
0
Control
7
14
28
Day
D
ESR in mm/hr
80
60
40
20
0
0
7
14
21
28
Day
E
Body Temp in °F
107
106
105
104
103
102
101
0
7
14
21
28
Day
F
Relative Body Weight
100
95
90
85
80
75
0
7
14
21
28
Day

FIG. 22.

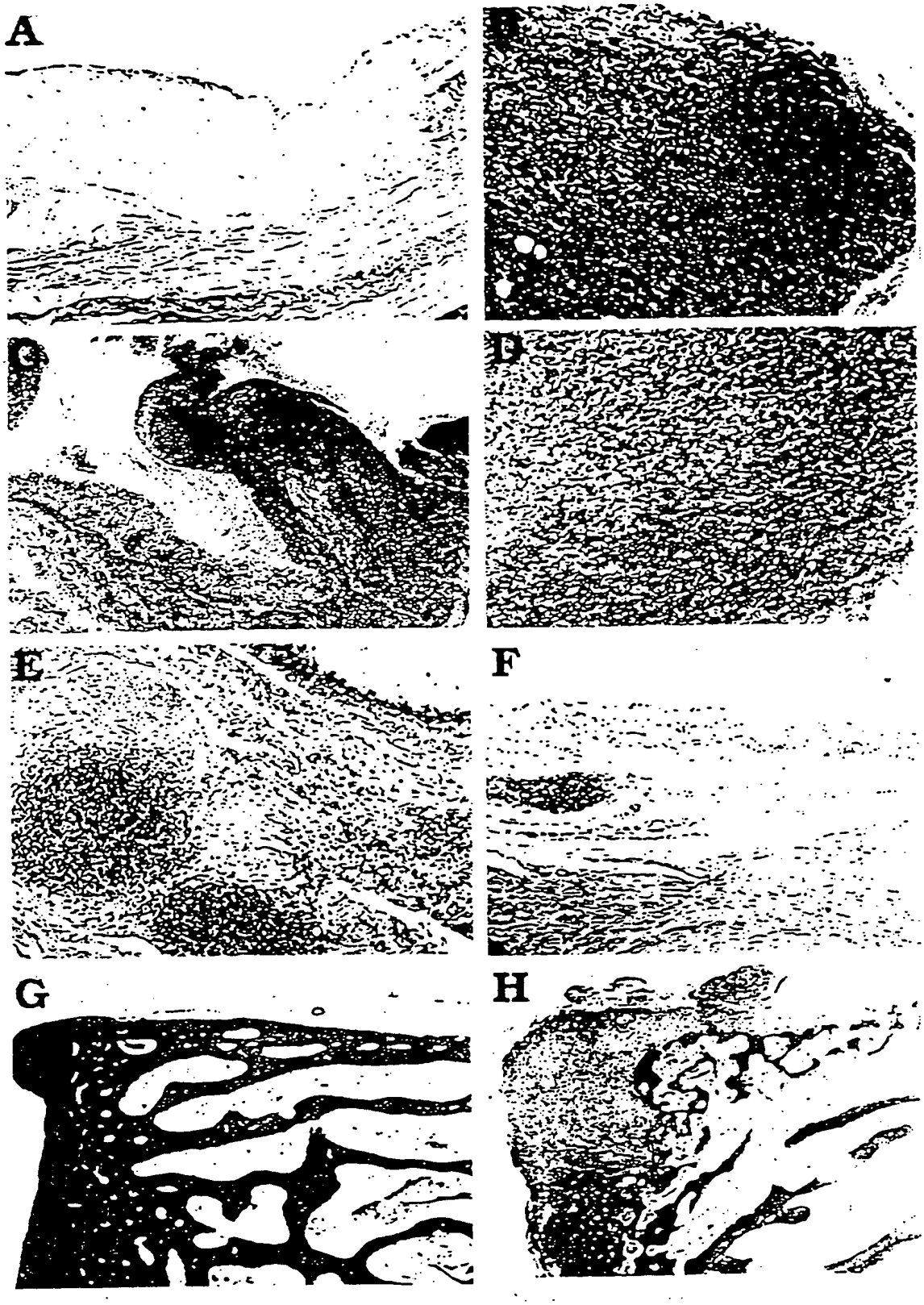


FIG. 23.

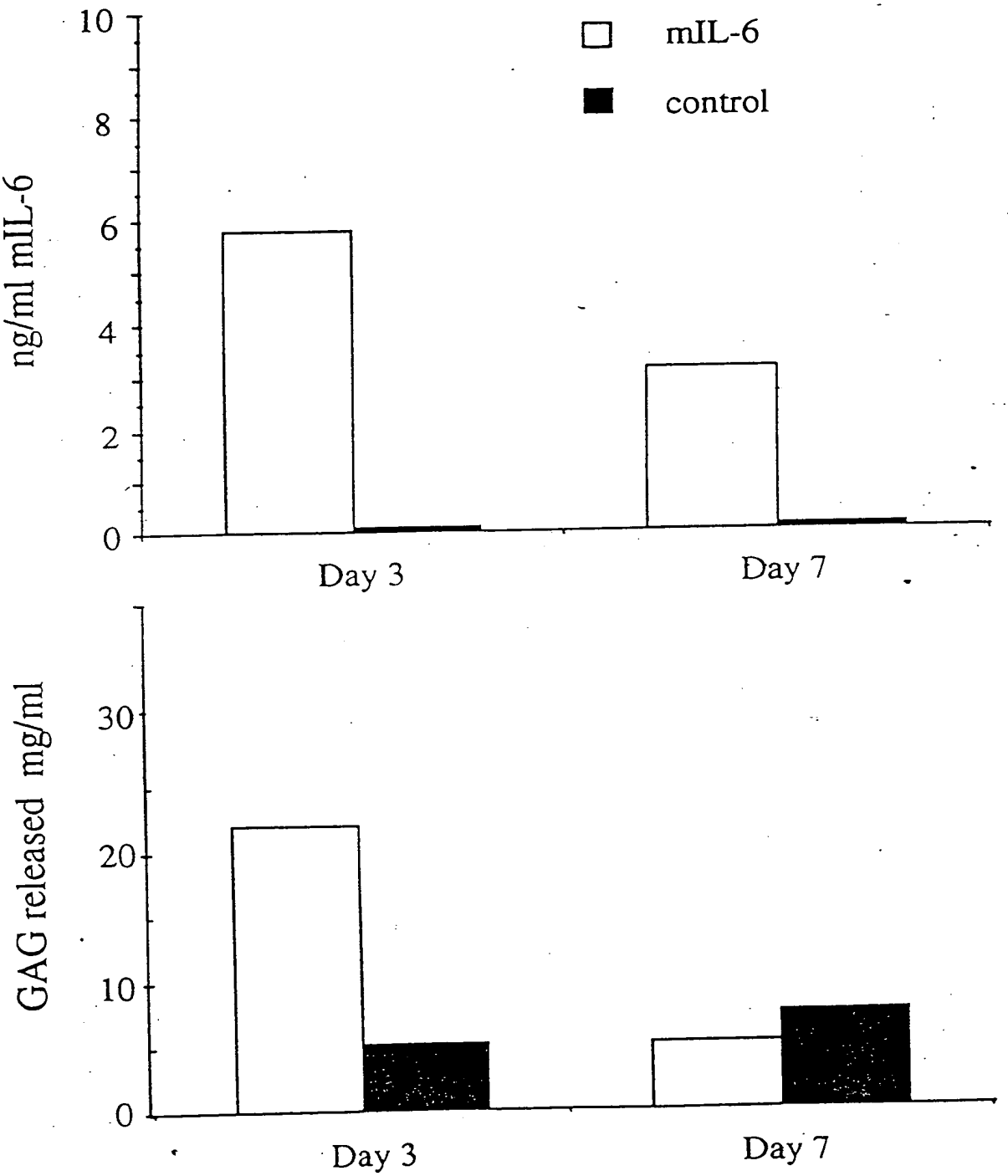

mIL-6
control
ng/ml mIL-6
10
8
6
4
2
0
Day 3
Day 7
GAG released mg/ml
30
20
10
0
Day 3
Day 7

FIG. 24.

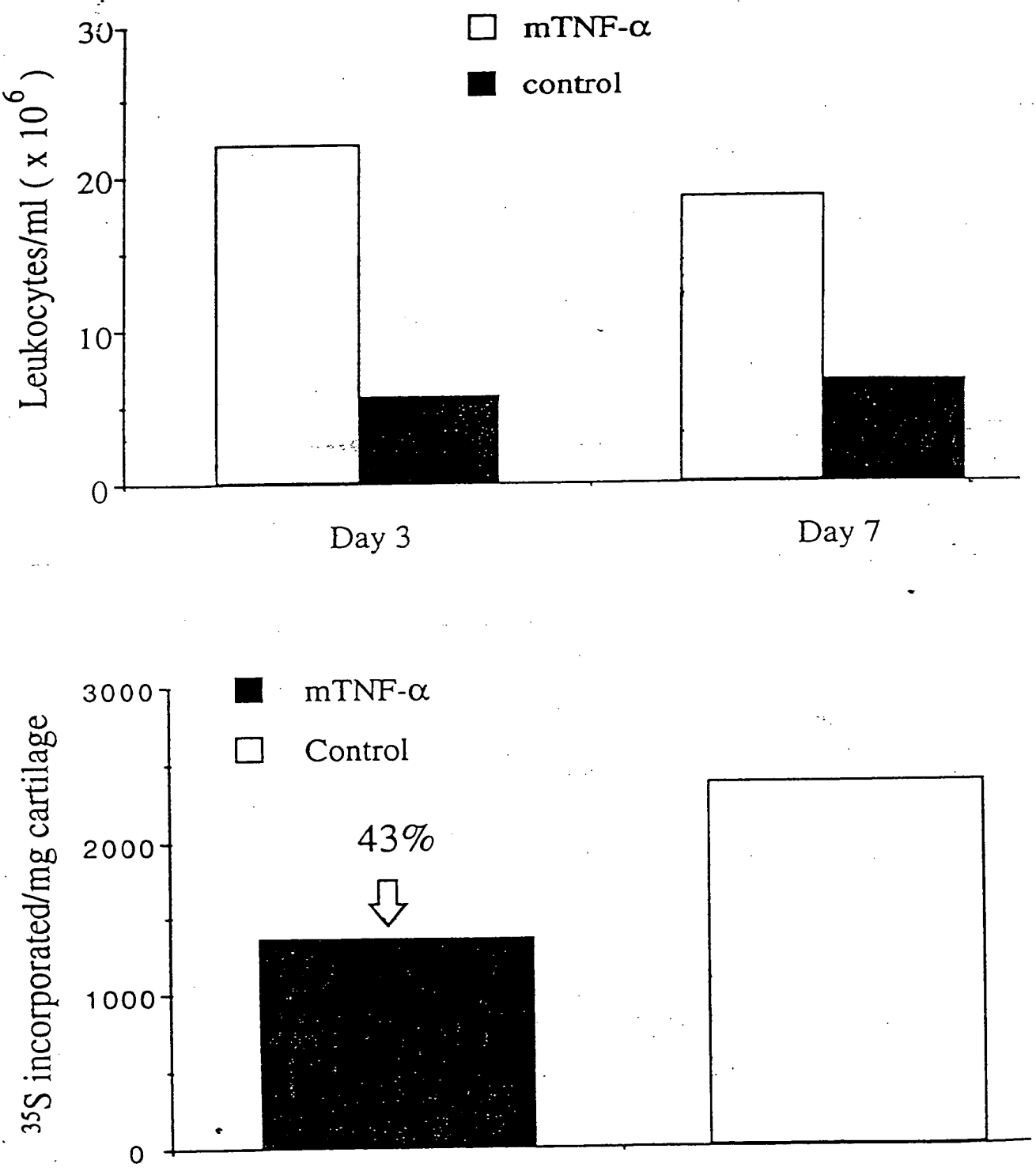

mTNF-α
control
Leukocytes/ml (x 10^6)
30
20
10
0
Day 3
Day 7
mTNF-α
Control
43%
35S incorporated/mg cartilage
3000
2000
1000
0

FIG. 25.